



Production of pyridinecarboxy aldehydes, nicotinic and isonicotinic and picolinic acids by TiO_2 -sacrificial photocatalysis at ambient conditions and in aqueous solution through artificial solar radiation

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ABSTRACT

The conversion of pyridinemethanol isomers into their respective aldehydes and carboxylic acids has been attempted in aqueous solution through sacrificial TiO_2 photocatalysis in the presence of cupric ions, at ambient temperature, under acidic and deaerated conditions, using artificial sunlight.

The presence of a nitrogen atom in the aromatic ring, with respect to benzyl alcohol and its derivatives, affects the photocatalytic behavior of the substrate. The influence of both pH and temperature has also been investigated. The position of the methanolic group on the aromatic ring leads to slight changes in the selectivities, yields and the oxidation rates. Under the adopted conditions, the yields and selectivities to aldehydes are always higher than those of the respective carboxylic acids.

The photocatalytic process can be carried out in consecutive copper reduction/oxidation steps in order to reuse the catalyst. In this way greater yields and selectivities to the desired product than 60% can be achieved.

The process can be considered interesting as it concerns the eco-green production of valuable fine chemicals, using water as a solvent at ambient conditions, a cheap heterogeneous catalyst and solar radiation.

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1. Introduction

Nicotinic, isonicotinic and picolinic acids are valuable intermediates for pharmaceuticals, dyes, agriculture products, and in the production of cosmetics and food additives [1–3].

Nicotinic acid (niacin, vitamin PP or B3) is an important vitamin in the B group: it is particularly used in the prevention and treatment of pellagra disease. The annual worldwide production of nicotinic acid is around 35,000 tons [4].

Pyridinecarboxylic acids are industrially produced through the oxidation of the respective picolinic isomers with nitric acid, permanganate or chromic acid under high pressure in the liquid-phase or by means of vapor-phase oxidation with oxygen or air over supported catalysts, such as vanadia–titania–zirconia oxides [5,6,59].

Pyridinecarboxylic acids are also formed via the hydrolysis of pyridinecarboxynitriles, which are produced by the ammonoxidation

of picoline isomers in the presence of solid catalysts [7,8] or using nitrile hydratase–amidase enzymatic systems [58]. However, some of these processes suffer from substantial drawbacks. The main disadvantages of liquid-phase processes include problems due to the handling of nitric acid at elevated temperatures and pressures, and to the production of mother-liquors, caused by the neutralization of nitric acid, together with the purity of the end-products [9]. On the other hand, catalyzed vapor-phase processes suffer from problems due to the necessity of obtaining a selective and efficient reaction, because of the existence of undesired competitive total oxidation reactions of the reagents and intermediates, and catalyst regeneration [4]. Moreover, from a safety point of view, both the liquid and vapor of picoline derivatives, which are used as reagents, are highly flammable and spread quite readily over an operating system [10,11].

These problems have led to the search for alternative routes and manufacturing processes that are less expensive and dangerous and no-polluting for pyridine carboxylic acids [12].

For example, the one-pot synthesis of nicotinic acid by air oxidation of 3-picoline over a $\text{V}_2\text{O}_5\text{-TiO}_2$ catalyst has been proposed

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[13–15]. 3-picoline can also be oxidized with oxygen, in the gas-phase, to nicotinic acid, with high yields on mixed oxide catalysts, such as $\text{Cr}_{1-x}\text{Al}_x\text{VO}_4$ or $\text{CrV}_{1-x}\text{P}_x\text{O}_4$ [16,17]. These processes produce little solid or liquid waste and no harmful gas exhaust, and thus meet all the requirements of “green” technology, although operative temperatures equal to or higher than 250 °C are required.

Moreover, it has been reported that methylpyridine isomers are stable at high temperatures, but pyridine-carboxylic acids, pyridine-carboxaldehydes and pyridylmethanol intermediates all undergo cleavage and form pyridine with the release of carbon dioxide, formic acid and formaldehyde, respectively [18].

Cobalt-doped catalysts and selenium dioxide also exhibit very high picoline conversion and good selectivity towards to pyridinecarboxylic acids in organic solvents [6,19]. In this case, the main disadvantage is the handling of highly toxic poisonous and expensive metals. It has been demonstrated that methylpyridine isomers can be effectively converted to pyridinecarboxaldehyde isomers through a photocatalytic oxidation process using TiO_2 as the catalyst under deaerated conditions [20]. The pyridinecarboxaldehyde production rate depends on which TiO_2 powder is used and on the position of the methyl group in the pyridinic ring.

In recent years, TiO_2 photocatalysis has also been successfully proposed in a selective oxidation process of aromatic alcohols to aldehydes and carboxylic acids, and high yields have been obtained [21–25,60]. Among the photocatalytic processes that have the aim of partially oxidizing aromatic alcohols, “sacrificial photocatalysis”, in which oxygen is replaced by cupric ions dissolved in the solution to prevent the mineralization to CO_2 , is particularly interesting [26,27]. The cupric ions are reduced to a lower oxidation state by capturing the photo-generated electrons on TiO_2 , whereas the alcohol is oxidized, through a direct reaction with the positive holes [28].

Among the TiO_2 commercial samples that were investigated, the catalysts in which TiO_2 is present in rutile form, either prevalently or totally, showed less activities than the samples that prevalently contain anatase [45], probably because the more negative redox potential (−0.27 V vs NHE) of the anatase conduction band makes it more competitive than the rutile one (−0.15 V vs NHE) for cupric ion reduction.

At the end of the process, the solid TiO_2 photocatalysts can easily be recovered and recycled, while the cupric ions, after reduction to zero-valent copper, can be regenerated by means of air oxidation of metal copper under dark conditions.

In the present paper, the authors propose sacrificial photocatalysis as a green innovative method to produce pyridinecarboxaldehydes and pyridinecarboxylic acids, starting from their respective pyridinemethanol isomers.

The technique proposed can also be considered useful to produce pyridinecarboxy aldehydes, which are used as precursors for the synthesis of chemical agents with pharmacological or biological activities, such as antineoplastics, antivirals, antifungals, antibacterials and antimalarials [29–32].

Moreover, 2-pyridinecarboxyaldehyde is a precursor of pralidoxime, which is used to treat poisoning by organophosphates [33], while 4-pyridinecarboxyaldehyde is a chemical intermediate for the preparation of Donepezil [34], a drug used for the treatment of mild to moderate Alzheimer type dementia [35].

2. Experimental

2.1. Equipment

Photocatalytic runs have been carried out in a batch cylindrical glass jacketed reactor (280 ml) equipped with a high-pressure UV lamp (UV 12F-Helios Italquartz model, nominal power 125 W),



Fig. 1. Image showing the mixture before the photocatalytic process (A) and after 3 h of oxidation (B).

mainly emitting at 305, 313 and 366 nm (manufacturer's data). The measured powers of the lamp were 4.85×10^{-5} , 8.34×10^{-5} and $2.71 \times 10^{-4} \text{ E min}^{-1}$ at 305, 313 and 366 nm, respectively.

The reactor was thermostated at the desired temperature. The pH was regulated with perchloric acid and monitored by means of an Orion 420A+ pH-meter (Thermo).

Before starting each experiment, the solution was preventively purged with nitrogen to remove the oxygen present in the reactor. During the experimental runs, nitrogen gas was continuously sparged to the irradiated and magnetically stirred solution, thus preventing contact with the oxygen. **Fig. 1**.

Before the photocatalytic process, the solution and catalyst exhibited a slightly skyblue/white color due to the presence of titania and cupric aquo-complexes (A, **Fig. 2**). After the photocatalytic run, the mixture had a brown/red color (B, **Fig. 2**), thus indicating the presence of zero-valent copper.

2.2. Analytical methods

The 2-pyridinemethanol (2-PMA), 3-pyridinemethanol (3-PMA), 4-pyridinemethanol (4-PMA), 2-pyridinecarboxyaldehyde (2-PCA), 3-pyridinecarboxyaldehyde (3-PCA), 4-pyridinecarboxaldehyde (4-PCA), nicotinic (NA), isonicotinic (INA) and picolinic

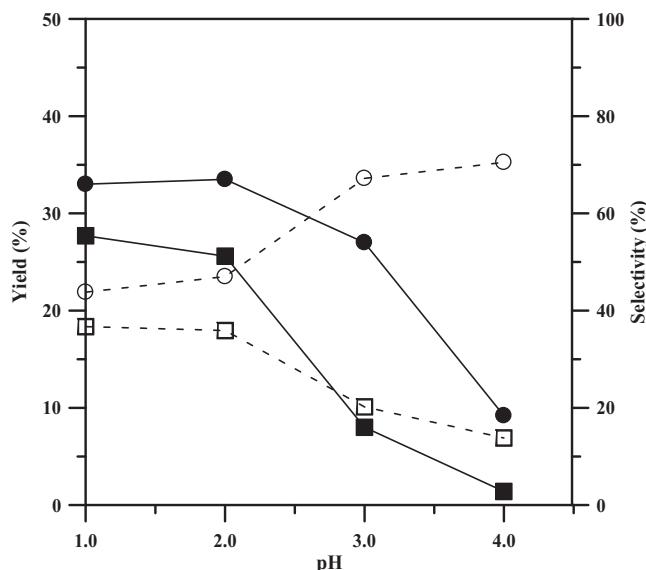


Fig. 2. Effect of pH on the yields (full symbols) and selectivities (empty symbols). $[3\text{-PMA}]_0 = 1.5 \text{ mM}$, $[\text{Cu(II)}]_0 = 1.5 \text{ mM}$, initial TiO_2 load = 200 mg, $T = 25^\circ\text{C}$. Reaction time: 3 h. Lamp ON. Yield: 3-PCA (●), NA (■); Selectivity: 3-PCA (○), NA (□).

(PIA) acid concentrations (Table 1) were evaluated at different reaction times through HPLC analysis. For this purpose, the HPLC apparatus (Agilent 1100) was equipped with a diode array UV-vis detector ($\lambda = 265 \text{ nm}$) and a Syngi 4u MAX-RP 80A (Phenomenex) column, using a mobile phase of acetonitrile (A) and a buffer solution (B) constituted by 20.0 mM of ammonium acetate dissolved in water for HPLC, flowing at 1.0 ml min^{-1} . A linear gradient was adopted starting with 5% A to 25% A, from the 5th to the 15th minute of each analysis, with a subsequent re-equilibrium time of

Table 1
Structure formulas of the investigated compounds.

Structure, name and pK_a		Products	
Reagents			
Alcohols			
2-Pyridinemethanol (2-PMA) $\text{pK}_a: 4.90 \text{ (NH)}$ [37]			
3-pyridinemethanol (3-PMA) $\text{pK}_a: 5.2 \text{ (NH)}$ [41]			
4-pyridinemethanol (4-PMA) $\text{pK}_a: 5.7 \text{ (NH)}$ [43]			
		Carboxylic acids	

4 min, which was necessary to reach the initial conditions (5% A and 95% B). The cupric ion concentration was measured, through a colorimetric method, using an analytical kit (based on oxalic acid bis-cyclohexylidene hydrazide, cuprizone®) purchased from Macherey-Nagel. A UV-vis spectrophotometer (ATi-Unicam) was used for the measurements at a wavelength of 585 nm.

The total organic carbon (TOC) was monitored by means a TOC analyzer (Shimadzu 5000 A).

X-ray diffraction (XRD) patterns of TiO_2 samples were collected using a Philips X'Pert PRO apparatus with $\text{Cu K}\alpha$ radiation: the scanning range was $5\text{--}80^\circ$ in 2θ , the scanning step size was 0.013° , and the scan speed was $0.164^\circ \text{ s}^{-1}$.

2.3. Materials

TiO_2 Aldrich (pure anatase phase, BET specific surface area $9.5 \text{ m}^2 \text{ g}^{-1}$, $\text{pH}_{\text{ZPC}} 4.2$ [36]) was used as the photo-catalyst. Cu(II) ions were introduced into the system as cupric perchlorate. All the reagents were purchased from Sigma Aldrich and used as received.

3. Results and discussion

The experimental investigation was carried out to assess the influence of some operative conditions (pH, temperature and initial Cu(II) concentration) and the nature of the reagents (presence of nitrogen aromatic ring, substituent position) on the selectivities and yields of the photocatalytic partial oxidation process.

3.1. Influence of pH

Partial photocatalytic oxidation runs were carried out, using 3-PMA as the reagent, in order to assess the effect of pH on the system efficiency, in terms of selectivity and yield. The results,

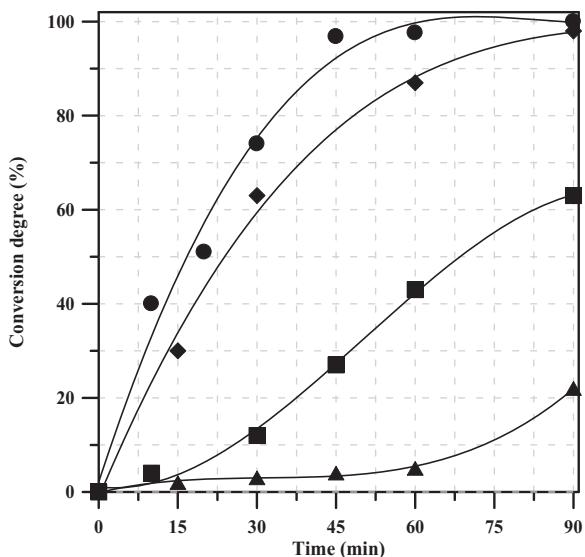
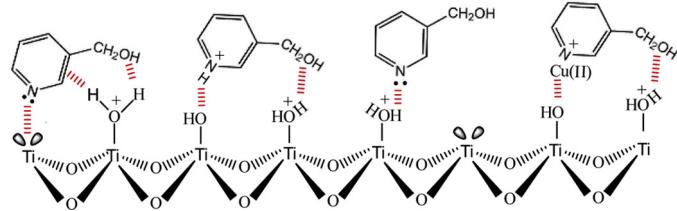


Fig. 3. Effect of pH on the Cu(II) conversion degree. $[3\text{-PMA}]_0 = 1.5 \text{ mM}$, $[\text{Cu(II)}]_0 = 1.5 \text{ mM}$, initial TiO_2 load = 200 mg, $T = 25^\circ\text{C}$. Lamp ON. pH: 1.0 (●), 2.0 (◆), 3.0 (■), 4.0 (▲).

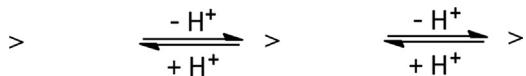
reported in Fig. 2, indicate an increase in the selective oxidation to 3-PCA (empty circles) and a decrease in NA (empty squares) with an increase in pH to 4.0, whereas the yields decrease from 33% to 9% for 3-PCA (black circles) and from 28% to 2% for NA (black squares) after 3 h of reaction.

The conversion degree of cupric ions decreases when the pH is changed from 1.0 to 4.0 (Fig. 3). A similar trend was previously observed for the selective TiO_2 -photoassisted oxidation of benzyl alcohol to benzaldehyde [45].

On the basis of some findings found in the literature [46], it is possible to suggest that, for $\text{pH} < 4$, 3-PMA is adsorbed on the TiO_2 surface through hydrophobic-hydrophilic interactions, with the generation of binary and ternary complexes:



It can be observed, considering a pH_{ZPC} equal to 4.2 for the adopted titania powders [36]:



that an increase in the pH values from 1.0 to 4.0 drastically reduces the concentration of positive charges on the catalyst surface and partially inhibits the adsorption (and the reactivity) of 3-PMA ($\text{pK}_a = 5.2$).

In order to find a good compromise between the acceptable values of yield and selectivity, and pH values that are not too acidic, a pH of 2.0 was chosen for the subsequent experimental investigation.

The TiO_2 -photoassisted Cu(II) reduction, and the conversion of 3-PMA into 3-PCA and NA can mainly be explained considering the following reactions:



On the basis of the selectivity values that were found, it cannot be ruled out that the presence of hydroxyl radicals, which formed through the reaction of adsorbed water molecules or superficial hydroxyl groups with the photoinduced holes:



may react with 3-PMA, 3-PCA and NA to produce hydroxylated by-products.

3.2. Influence of aromatic nitrogen

It is known that the deaerated $\text{TiO}_2/\text{Cu(II)}$ -photoassisted partial oxidation of benzyl alcohol (BA) leads to benzaldehyde (BHA) and benzoic acid (BAC) [45]. For this reason, and with the aim of better understanding the role of the nitrogen atom present in the aromatic ring of 3-PMA and its derivatives, a comparison between 3-PMA and BA selective photo-oxidations was made under the same experimental conditions (Fig. 4a and b).

Observing Fig. 3a, it is clear that, when 3-PMA was used as a reagent instead of BA, higher conversion degrees were achieved (over 70% for 3-PMA and 60% for BA). Moreover, in the case of BA, when the cupric species were completely reduced to zero-valent copper, i.e. 70 min, no further consumption of benzyl alcohol was recorded. After 300 min of reaction time, the selectivities of oxidation reactions to BHA and BAC were 49.7% and 11.5%, respectively. On the other hand, a slight increase in the conversion degree, close to 10% for reaction times from 60 to 300 min, was observed for 3-pyridine-methanol, even though Cu(II) was totally converted to Cu(0), and resulted in a selective production of niacin.

Although the yields of oxidation to the corresponding aldehydes (BHA and 3-PCA) were very similar ($\approx 33\%$, full symbols in Fig. 4b), the photocatalytic partial oxidation of BA to BAC proceeded with lower yields (empty squares), i.e. 8% at 300 min, than those reached, under the same experimental conditions, for the selective conversion of 3-PMA to NA (empty circles), i.e. over 30% for prolonged reaction times. Once again, starting with 3-PMA as the substrate, a residual reactivity, which was measured as 3-PCA consumption (full circles) and NA production, was recorded when the Cu(II) species were no longer present in the solution, as they had acted as photoelectron scavengers.

The selectivities of oxidation to 3-PCA and NA, achieved at 300 min, were 43.6% and 41.3%, respectively. These results probably indicate the intervention of the photocatalytic selective oxidation reactions of 3-PMA to NA in which the Cu(II) species were not involved.

Some photocatalytic runs were carried out on 3-PMA and 3-PCA, under different experimental conditions, in order to confirm this hypothesis (Figs. 5a–c and 6).

Fig. 5a shows that the 3-PMA reactivity and its conversion degree are affected to a great extent by the presence of the Cu(II) ions and TiO_2 catalyst. No 3-PMA consumption occurs in the absence of the cupric species and titania powder, whereas an increase in the conversion degree to 17%, for a reaction time of 300 min, was observed in the presence of Cu(II) ions, but without TiO_2 . A similar result (14%) was recorded for a run carried out in the presence of TiO_2 , but without the Cu(II) species. It is necessary to point out that a marked reactivity increase was observed when both TiO_2 and Cu(II) were added to the solution, and a conversion degree close to 80% was reached for prolonged reaction times (Fig. 4a, full circles).

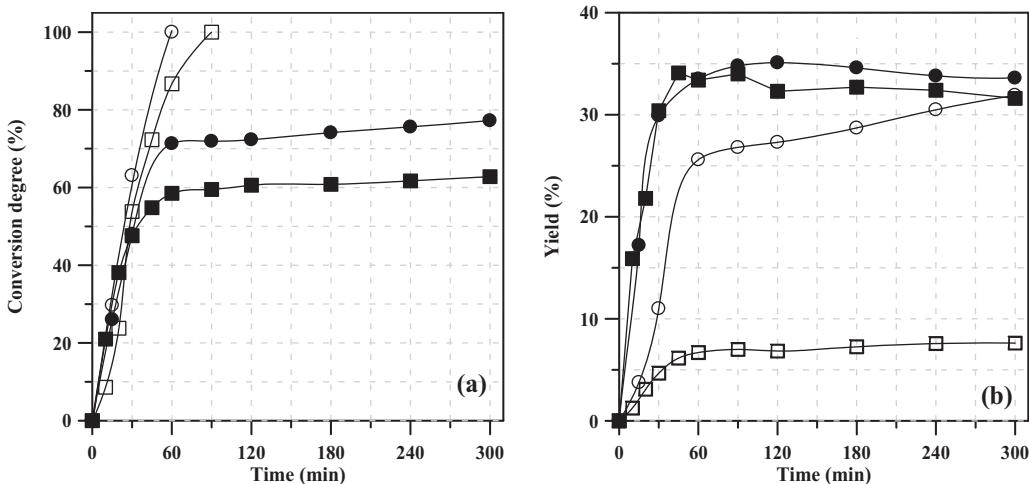


Fig. 4. Conversion degree (a) and yields (b) for different reaction times. $[BA]_0$, $[3\text{-PMA}]_0$, $[Cu(II)]_0 = 1.5\text{ mM}$, TiO_2 (200 mg), pH 2.0. $T = 25^\circ\text{C}$. Lamp ON. (a) $BA/Cu(II)/hv$: BA (■), Cu(II) (□); 3-PMA/Cu(II)/hv: 3-PMA (●), Cu(II) (○). (b): $BA/Cu(II)/hv$: BHA (■), BAC (□); 3-PMA/Cu(II)/hv: 3-PCA (●), NA (○).

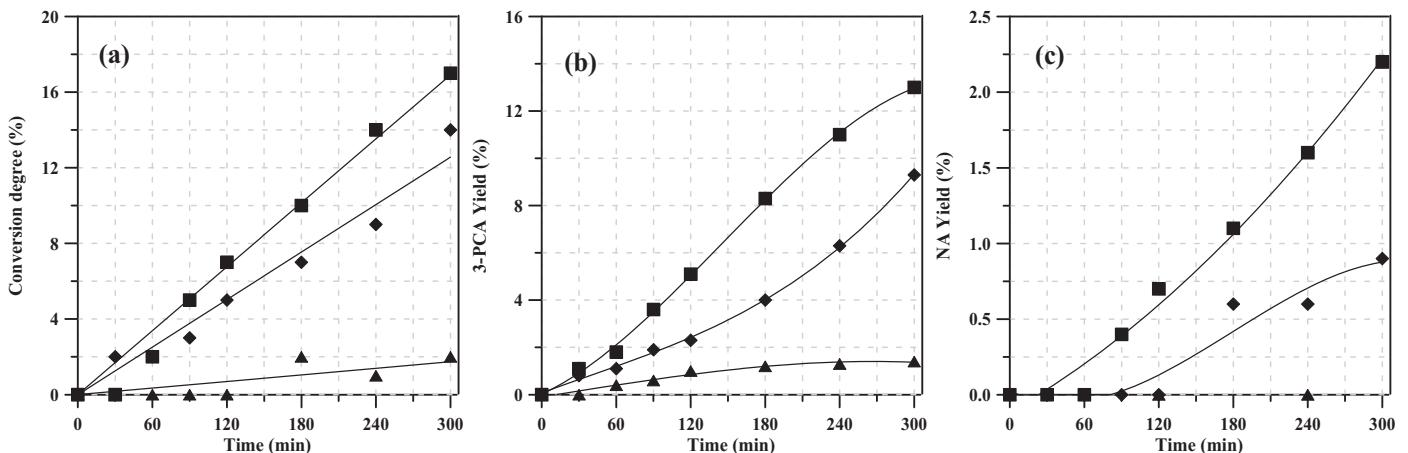


Fig. 5. Conversion degree of 3-PMA (a), yields to 3-PCA (b) and to NA (c) under different experimental conditions: $[3\text{-PMA}]_0 = 1.5\text{ mM}$, pH 2.0. $T = 25^\circ\text{C}$. Lamp ON. Direct photolysis (▲), only Cu(II) (1.5 mM) (■), only TiO_2 (200 mg) (◆).

As shown in Fig. 5b, the $Cu(II)/hv$ and TiO_2/hv processes gave yields of 3-PCA equal to 13.4% and 9.3%, respectively, for a reaction time of 300 min. Under the same experimental conditions, the $TiO_2/Cu(II)/hv$ system was characterized by a 3-PCA yield of 33.7% (Fig. 4b, full circles).

A further oxidation of 3-PCA to NA, which was carried out with $Cu(II)/hv$ and TiO_2/hv processes (Fig. 5c), occurred, but with very low yields compared to those (31.2% after 300 min) achieved using both the TiO_2 and $Cu(II)$ species (Fig. 4b, empty circles).

On the contrary, the $Cu(II)/hv$ and TiO_2/hv runs, carried out using benzyl alcohol as the reagent, instead of 3-pyridine-methanol, demonstrated that the former is completely unreactive under the same adopted conditions [45].

Additional experimental photocatalytic runs were carried out, starting with 3-PCA as the substrate. The conversion degrees of 3-PCA and the respective yields of oxidation to NA achieved for the $Cu(II)/hv$, TiO_2/hv and uncatalyzed systems are shown in Fig. 6. 3-PCA can be stoichiometrically photoconverted to NA in an aqueous solution containing only cupric ions or TiO_2 particles. No BHA conversion was measured under the similar conditions.

It is evident, from the collected results, that the presence of a nitrogen aromatic atom in the molecule (3-PMA, 3-PCA), with respect to the BA and BHA molecules, affects the photocatalytic behavior of the substrate to a great extent.

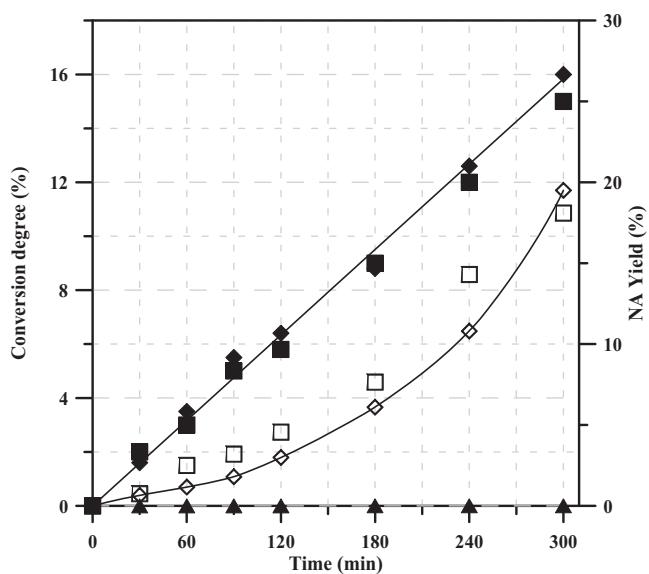


Fig. 6. Conversion degree of 3-PCA (full symbols), yields to NA (empty symbols) under different experimental conditions: $[3\text{-PCA}]_0 = 1.5\text{ mM}$, pH 2.0. $T = 25^\circ\text{C}$. Lamp ON. Direct photolysis (▲), only Cu(II) (1.5 mM) (■, □), only TiO_2 (200 mg) (◆, ◇).

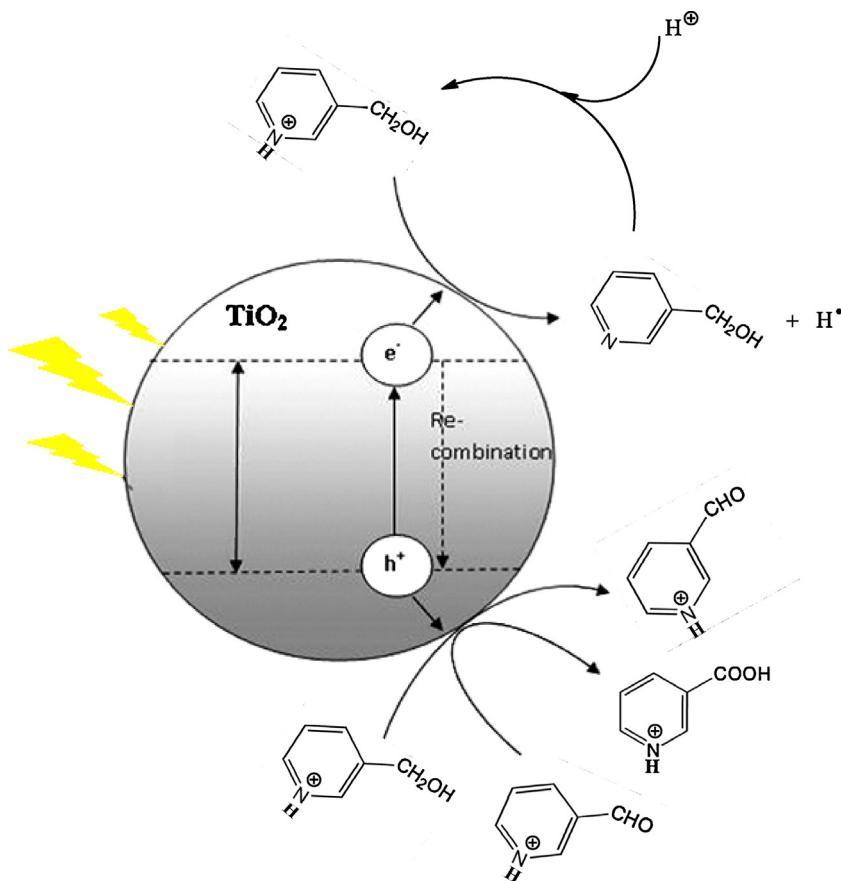
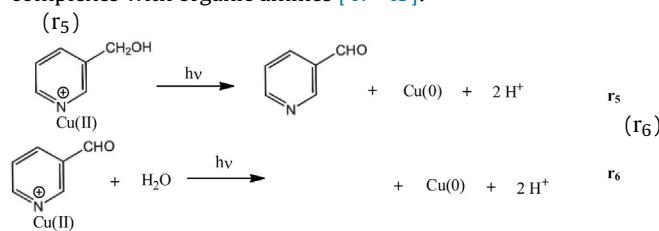


Fig. 7. Scheme of $\text{TiO}_2/\text{h}\nu$ photocatalytic selective oxidation of 3-PMA to 3-PCA and NA.

In the presence of only the Cu(II) species, without the TiO_2 photocatalyst, the complexes formed between 3-PMA or 3-PCA with cupric ions could undergo photoredox transformations, through an intramolecular electron transfer process, thus giving rise to cuprous ions or zero-valent copper and the respective 3-pyridine-carboxyaldehyde and nicotinic acid, in analogy to what has been reported for similar ligand-to-metal charge transfers of copper(II,I) complexes with organic amines [47–49]:



The photocatalytic system without Cu(II) species, but in the presence of TiO_2 particles, in which protonised 3-PMA and 3-PCA, adsorbed on the particles surface, as previously described, are able to react with photogenerated positive holes and/or photoelectrons, is more interesting. These molecules work as proton carriers, transporting protons from the liquid bulk to the surface of the particles. At the same time, 3-PMA and 3-PCA are selectively converted to 3-PCA and NA, respectively, as depicted in Fig. 7.

A similar role was previously ascribed to the catalytic effect of different protonated organic amines (aniline, benzylamine and peptides), dissolved in an acid aqueous solution, during the charge transfer process in the presence of platinum, mercury and copper electrodes [50–52].

This effect, known in the field of electrochemical reactions as “presodium” catalysis [53], is closely correlated to the protonisable nature (lone electron pair) of the aromatic nitrogen atom, which is instead absent in the BA molecule, and thus results to be unreactive under the same operative conditions. On this occasion, the above term has been modified and readapted by the authors to “presodium” photocatalysis, in order to denote the catalytic action of an organic species (carrier) in promoting proton photoreduction by mediating its transfer from the bulk solution to the photocatalyst surface.

The occurrence of r_5 and r_6 reactions and those reported in Fig. 7, in addition to r_2 and r_3 reactions, due to the presence of a pyridine nitrogen atom, implies higher conversion degrees for the system, starting from 3-PMA, compared to those achieved using BA as the reagent.

Furthermore, the carbon balances, calculated as the sum of the alcohol, aldehyde and carboxylic acid concentrations measured at different reaction times and normalized with respect to the initial alcohol concentration, showed that the process was more selective when 3-PMA was used instead of BA (Fig. 8). In fact, the mass balances closed with 88% and 75%, respectively, when 3-PMA and BA were used as the starting reagents. Moreover, additional total organic carbon analyses carried out on samples taken after 60, 120 and 180 min of photocatalytic oxidation of 3-PMA, indicated a TOC removal degree close to 8.0–8.4% for the same adopted experimental conditions. These results have demonstrated that the calculated loss of carbon (12% for 3-PMA) can mainly be ascribed to the formation of carbon dioxide, due to the occurrence of side $\text{HO}\cdot$ -mediated reactions.

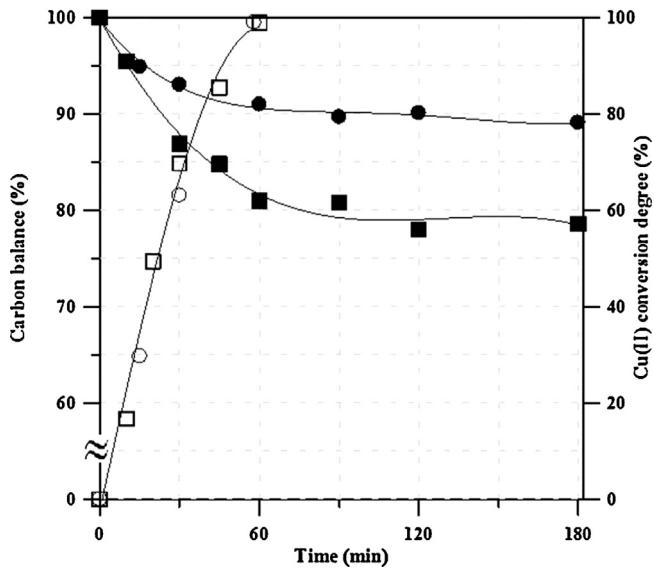


Fig. 8. Carbon balances (full symbols) and cupric ions conversion degree (empty symbols) for 3-PMA (●, ○) and BA (■, □) with $\text{Cu(II)}/\text{TiO}_2/\text{h}\nu$ system. $[\text{BA}]_0$, $[\text{3-PMA}]_0$, $[\text{Cu(II)}]_0 = 1.5 \text{ mM}$, TiO_2 (200 mg), pH 2.0, $T = 25^\circ\text{C}$. Lamp ON.

3.3. Effect of initial Cu(II) concentration

Figs. 9a–c show the conversion degrees of 3-PMA and the yields of oxidation to 3-PCA and NA that were reached for different reaction times, during the photocatalytic partial oxidation runs, keeping constant the starting 3-PMA concentration (1.5 mM) and TiO_2 load (200 mg/l), but for different initial Cu(II) concentrations. When the Cu(II) concentration is moved from 0.9 to 3.8 mM, the system reactivity increases remarkably and conversion degrees close to 100% are obtained (Fig. 9a).

For higher reaction times than 30 min, a higher initial cupric ion concentration results in a decrease in the 3-PCA yield (Fig. 9b) and an increase in the yield to NA (Fig. 9c). In the presence of large amounts of Cu(II) ions, more photogenerated electrons are scavenged (r_2) and a further oxidation of 3-PCA can be observed (r_3), due to the build-up of the holes that have formed. Moreover, when the starting cupric ion concentrations are increased, the photoredox transformations of the 3-PMA-Cu(II) and 3-PCA-Cu(II) complexes are enhanced (r_5 and r_6).

As shown in Fig. 10, the selectivity of the reaction to 3-PCA is reduced when the $[\text{Cu(II)}]_0/[\text{3-PMA}]_0$ feed ratio increases, i.e. the

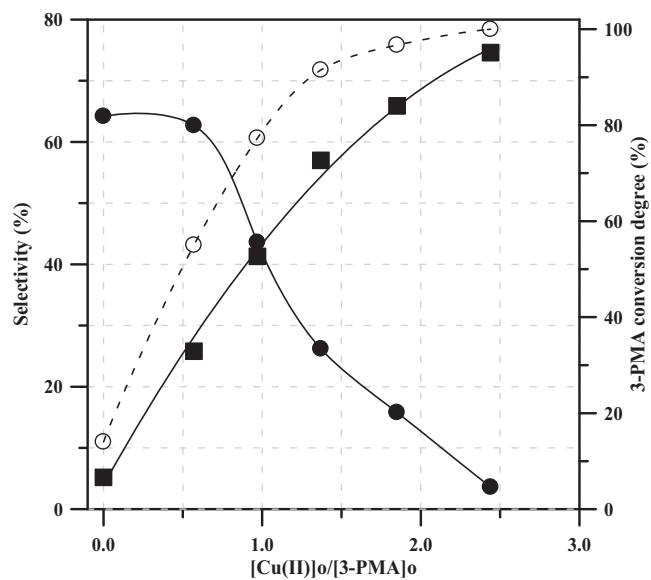


Fig. 10. Effect of initial $[\text{Cu(II)}]_0/[\text{3-PMA}]_0$ feed ratio on the 3-PCA and NA selectivities and 3-PMA conversion degree. TiO_2 load = 200 mg, pH 2.0, $T = 25^\circ\text{C}$. Reaction time (5 h). Lamp ON. Selectivities (full symbols, continuous line): 3-PCA (●), NA (■); 3-PMA conversion degree (○, dashed line).

initial Cu(II) concentration at fixed $[\text{3-PMA}]_0$. On the other hand, 3-PMA can be converted completely after 300 min, and a selectivity to NA of 75% can be achieved by adopting a $[\text{Cu(II)}]_0/[\text{3-PMA}]_0$ feed ratio of 2.44.

3.4. Effect of temperature

The influence of temperature on the partial oxidation of 3-PMA, through a TiO_2 -sacrificial solar simulated process, has also been studied. The results, which are not shown, were collected at three different temperatures (15, 25 and 35°C), and evidenced that the system reactivity and the reaction yields to 3-PCA and NA were not affected by changes in the temperature. Within the temperature range explored, the 3-PMA conversion degree and the selectivities of oxidation reactions to 3-PCA and NA, after 1 h of reaction time, that is, when the Cu(II) species were totally reduced, reached values close to 70%, 50% and 35%, respectively, under the adopted experimental conditions (pH 2.0, TiO_2 load = 200 mg/l and 3-PMA/Cu(II) feed molar ratio = 1). The results are consistent with those found in the literature according to which heterogeneous photocatalytic

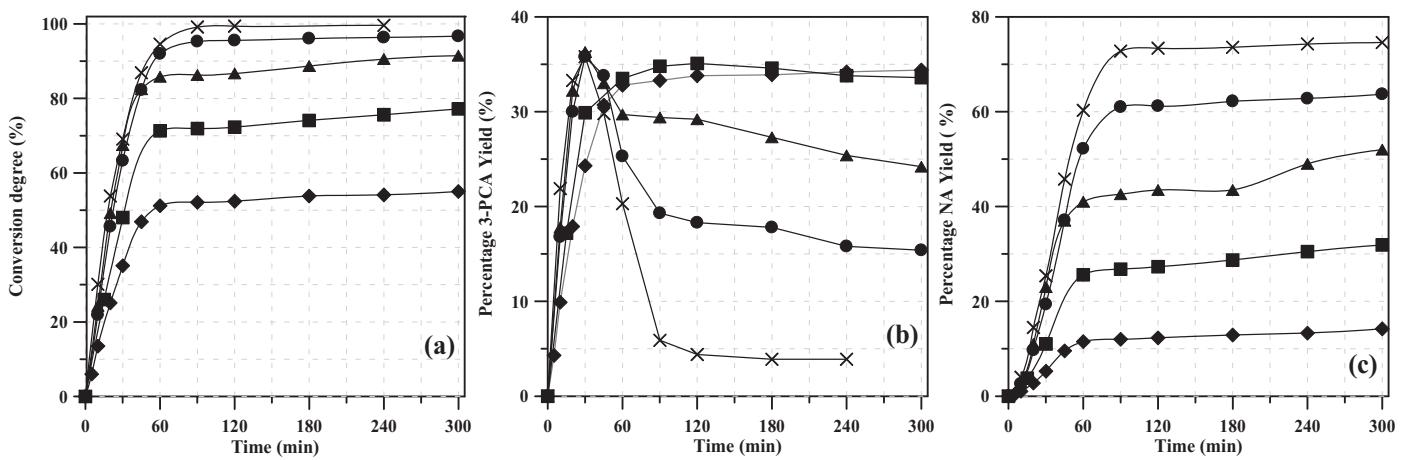


Fig. 9. Conversion degree of 3-PMA (a), yields to 3-PCA (b) and NA (c) at varying initial Cu(II) concentrations. $[\text{3-PMA}]_0 = 1.51 \text{ mM}$, initial TiO_2 load = 200 mg, pH 2.0, $T = 25^\circ\text{C}$. Lamp ON. $[\text{Cu(II)}]_0$ (mM): 0.91 (◆), 1.51 (■), 2.12 (▲), 2.91 (●), 3.81 (×).

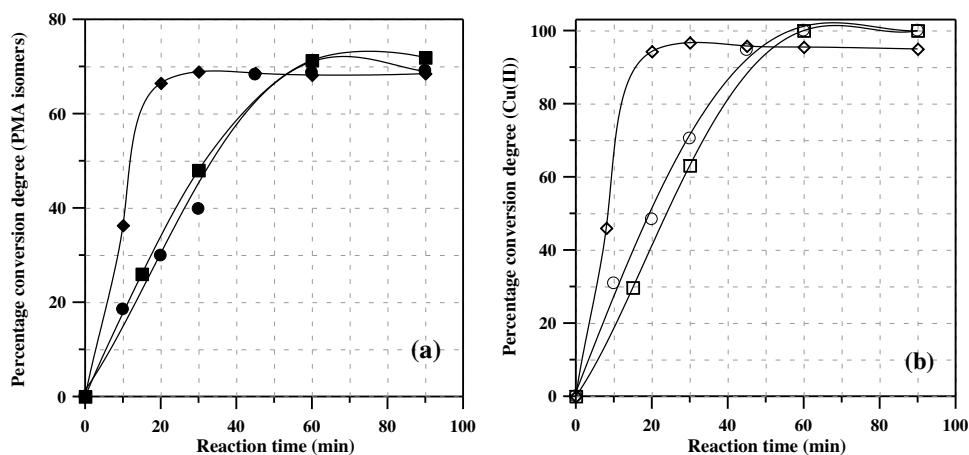


Fig. 11. Conversion degrees of PMA isomers (a) and cupric ions (b). $[x\text{-PMA}]_0 = 1.5 \text{ mM}$, $[\text{Cu(II)}]_0 = 1.5 \text{ mM}$. TiO_2 load = 200 mg, pH 2.0, $T = 25^\circ\text{C}$. Lamp ON. 2-PMA (●), Cu(II) (○); 3-PMA (■), Cu(II) (□); 4-PMA (◆), Cu(II) (◇); x: 1-, 2- or 3-

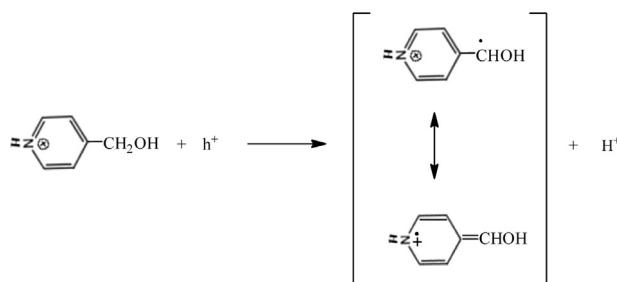
reactions are not affected to any great extent by moderate variations in temperature [54,55]. This behaviour can mainly be ascribed to the fact that:

- (1) All the reactions contributing to the TiO_2 -photocatalytic investigated process are represented by radical-type steps that have low activation energies and, therefore, should not be affected significantly by changes in temperatures.
- (2) The activation energy of the catalyst in the investigated temperature range is negligible ($kT = 25\text{--}27 \text{ meV}$) [56].

3.5. Effect of the methanolic group position

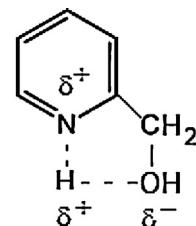
The conversion degrees of the ortho, meta and para isomers of pyridine-methanol, along with the cupric ions, are compared in Fig. 11a and b.

The final conversion degree of PMA is close to 70% for all three isomeric species, whereas the Cu(II) species are reduced completely. The results have pointed out a greater tendency of 4-PMA (◆, ◇) to oxidize than the respective 2-PMA and 3-PMA isomers. In other words, the order of the conversion rates is $\nu_{4\text{-PMA}} > \nu_{3\text{-PMA}} \approx \nu_{2\text{-PMA}}$. Similar results were also found for electron transfer reactions on analogues pyridine derivatives [39]. The higher reactivity of the para isomer, as suggested, can be explained by considering the increased stability of the radical species formed from 4-PMA compared to the ortho and meta isomers. This finding is based on the resonance structures, with a positive charge on the nitrogen atom and the unpaired electron:



Although a similar resonance occurs in the ortho isomer, the inductive effect of the nitrogen (electron-attracting) and the presence of an intramolecular hydrogen bond, which oppose the resonance phenomena, are particularly important in the ortho

position of the methanolic group:



The yields to the respective aldehydic (x-PCA) and carboxylic (x-PA) derivatives are reported in Fig. 12. The highest value for the pyridine carboxy aldehyde isomers (full symbols) was achieved for the ortho isomer, while the lowest was reached for the para one. It is worth noting that the maximum values of yield for the 2-PCA and 4-PCA isomers were obtained for reaction times in which the cupric ions were converted completely. Afterwards, both the ortho and para carboxy aldehydes, unlike the meta one, were only consumed slightly. This difference may tentatively be ascribed to the direct photolysis of the 2-PCA and 4-PCA compounds, as experimentally verified (data not shown). On the other hand, under the same conditions, i.e. only radiation, without the cupric species or titania dioxide, it was previously reported that 3-PCA remained completely unreactive (Fig. 6, full triangles). The oxidation yields to the respective carboxylic acids (x-PA) were close to 15%, and the carboxylic acids were no longer reactive.

The yields (Y) and selectivities (S) for the PCA and PA isomers, obtained through the partial photocatalytic oxidation of the PMA isomers, are reported in Table 2 in order to provide a comparison of the investigated substances. The values refer to a reaction time of 45 min, that is, when a Cu(II) conversion of 90% was achieved for all three isomers. It can be observed that both the Y and S values of the aldehydes are always higher than those of the respective carboxylic acids.

3.6. Copper reuse

In order to evaluate the possibility of reusing copper and increasing the yield of the carboxylic acid derivative, a photocatalytic process was carried out, starting from 3-PMA, for three consecutive cycles, by reoxidizing the zero-valent copper to cupric ions in the dark with oxygen each time (Fig. 13a and b).

The reaction time for the first and second deaerated photocatalytic steps was 90 min long (blank zone), whereas the third

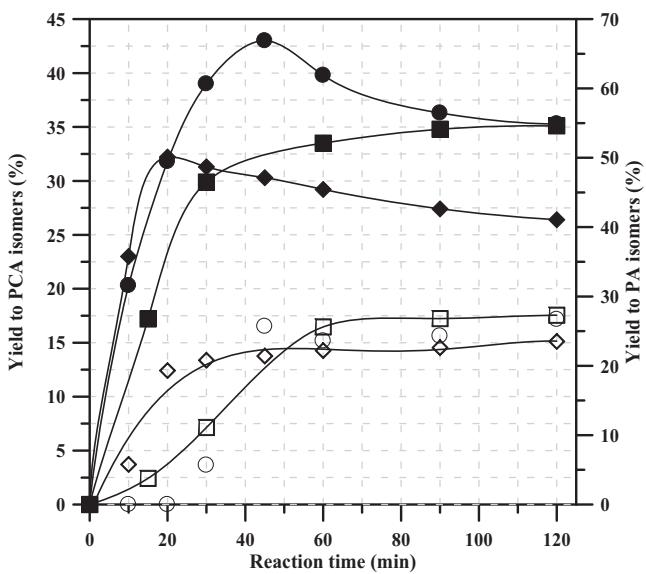


Fig. 12. Yields to PCA and PA isomers for various reaction times. $[x\text{-PMA}]_0 = 1.5 \text{ mM}$, $[\text{Cu(II)}]_0 = 1.5 \text{ mM}$, TiO_2 load = 200 mg, pH 2.0, $T = 25^\circ\text{C}$. Lamp ON. 2-PCA (●), 2-PA (○), 3-PCA (■), 3-PA (□); 4-PCA (◆), 4-PA (◇).

one was 180 min. During the first photocatalytic step, conversion degrees of 43% and 100% were achieved, respectively, on the 3-PMA and Cu(II) species (Fig. 13a). The oxidation yields to 3-PCA and NA, for the same reaction time, were 30% and 8%, respectively (Fig. 13b).

A reoxidation of zero-valent copper to cupric ions was then carried out by means of oxygen bubbling in the dark (red zone). During this step, a 3-PMA conversion of 11% was recorded, with only a marginal increase in the 3-PCA and NA yields (32% and 13%) compared to the previous step. This additional consumption of 3-PMA may be ascribed to HO^\bullet formation through the radical reactions in which a copper cycle is involved between the cupric and cuprous oxidation states [57]:

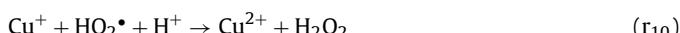
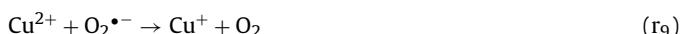
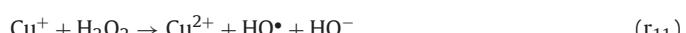


Table 2

Yields (Y) and selectivities (S) achieved after 45 min of reaction time. $[x\text{-PMA}]_0 = 1.5 \text{ mM}$, $[\text{Cu(II)}]_0 = 1.5 \text{ mM}$, TiO_2 load = 200 mg, pH 2.0, $T = 25^\circ\text{C}$. Lamp ON. The yields and selectivity were calculated as (moles of desired product)/(initial moles of alcohol) and (moles of desired product)/(moles of alcohol converted), respectively.

	$Y\text{ (%)}$	$S\text{ (%)}$
<chem>CN1CC=CC=C1C=O</chem>	43.0	62.9
<chem>CN1CC=CC=C1C(=O)O</chem>	25.7	37.6
<chem>CN1CC=CC=C1C=O</chem>	31.7	54.7
<chem>CN1CC=CC=C1C(=O)O</chem>	25.6	29.5
<chem>CN1CC=CC=C1C=O</chem>	30.3	44.0
<chem>CN1CC=CC=C1C(=O)O</chem>	21.4	31.2



The formed HO^\bullet species react unselectively with the substrates, partially producing 3-PCA and NA. The last step in the first cycle

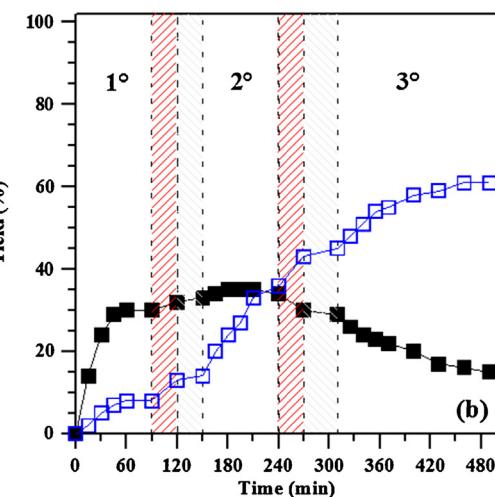
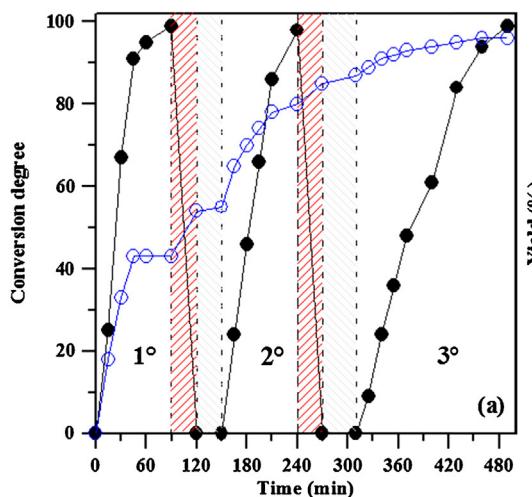


Fig. 13. Conversion degree (a) for Cu(II) species (●) and 3-PMA (○) and percentage yields (b) to 3-PCA (■) and NA (□) for three operative cycles. Blank zone: light on and nitrogen purge; Red zone: light off and oxygen purge; grey zone: light off and nitrogen purge. $[3\text{-PMA}]_0 = 1.71 \text{ mM}$, $[\text{Cu(II)}]_0 = 3.23 \text{ mM}$, initial TiO_2 load = 200 mg, pH 2.0, $T = 25^\circ\text{C}$. Lamp ON (For interpretation of the color information in this figure legend, the reader is referred to the web version of the article.).

was a purge with nitrogen gas, in the dark, to remove the residual oxygen dissolved in the aqueous solution (yellow zone). No reagent consumption was recorded. Two further photocatalytic cycles were performed, adopting the same sequence of steps.

After the second photocatalytic irradiation step, the 3-PMA conversion and the 3-PCA and NA yields were 80%, 34% and 36%, respectively. Finally, at the end of the 3rd photocatalytic step, an almost complete conversion on 3-PMA was observed, whereas the yield and selectivity of the process to nicotinic acid were 61% and 64%, respectively.

An additional XRD analysis was performed on the TiO₂ samples before and after the photocatalytic process, but it did not show any modification of the titania (anatase) crystalline phase. These results demonstrate the possibility of carrying out the process in consecutive copper reduction/oxidation steps in order to recycle and reuse the catalyst. In this way, greater yields and selectivities to the desired product than 60% can be achieved.

4. Conclusion

Pyridinecarboxyaldehydes and pyridinecarboxylic acids can be obtained by means of artificial solar driven sacrificial TiO₂-photocatalysis, using pyridinemethanol isomers as reagents, in the presence of cupric ions at ambient temperature, in an acidic deaerated aqueous solution. Among the tested pyridinemethanol isomers, the highest yields and selectivities to aldehydic (43% and 63%) and carboxylic acid (26% and 38%) derivatives were reached by the ortho isomer. The photocatalytic oxidation rates and the yields were not influenced by temperature variations in the 15–45 °C range.

The presence of a nitrogen aromatic atom in the molecule, with respect to benzyl alcohol, have a marked effect on the photocatalytic behavior of the substrate. In this sense, the nitrogen atom acts as a “presodium” photocatalytic agent, that is, as a carrier that promotes proton photoreduction by mediating its transfer from the bulk solution to the photocatalyst surface.

The results have demonstrated that copper catalyst could easily be recycled and reused with air or oxygen in dark conditions. The proposed process can be considered an attractive example of the eco-green synthesis of pharmacological active compounds, compared to the current industrial processes for the production of nicotinic acid and its derivatives. In fact, the very mild operative conditions adopted, i.e. water as the solvent, ambient temperature, cheap heterogeneous catalyst, and sunlight radiation, make the system rather interesting for the future commercial solar-driven production of vitamin B3 and its derivatives.

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